Cutaneous, pulmonary and sinusal aspergillosis in a diabetic patient

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Aspergillose cutanée, pulmonaire et sinusienne chez une patiente diabétique

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RÉSUMÉ

Prérequis : L'aspergillose cutanée est rare chez les diabétiques.
But : Le but de notre travail est de rapporter un cas d'aspergillose disséminée à évolution fatale révélée par des lésions nécrotiques cutanées multiples, associées à une atteinte pulmonaire et sinusienne chez une patiente diabétique.
Observation: Patiente âgée de 60 ans, diabétique, s'est présentée avec des nécroses cutanées rapidement extensives de 1 à 10 cm qui évoluaient depuis un mois au niveau du tronc, des membres et des paupières. Quelques jours après son admission, elle a présenté une dyspnée avec à la radiographie thoracique un syndrome alvéolo-interstitiel et de multiples opacités excavées. Le scanner facial a montré une cellulite orbitaire droite et une pansinusite. La coloration au Gomori-Grocott sur la biopsie cutanée a montré des filaments mycéliens ayant des branches à angles droits. L'immunofluorescence avec un serum anti-aspergillaire était positive. Le diagnostic d'aspergillose disséminée secondaire à un foyer primaire pulmonaire avec une dissémination cutanée, sinusienne et des voies respiratoires supérieures a été posé. La patiente est rapidement décédée malgré un traitement par amphotericine B.
Conclusion : Notre cas soulève l'importance d'évoquer et de rechercher une mycose profonde devant toute nécrose ou ulcération cutanée survenant chez un sujet immunodéprimé. Le pronostic dépend du délai diagnostic et thérapeutique.

SUMMARY

Background : Cutaneous aspergillosis is rarely reported in diabetic patients.
Aim : The objective of our study is to report a case of lethal disseminated aspergillosis revealed by multiples skin necroses, with pulmonary and sinusal involvement in a diabetic patient.
Case report: A 60-year-old diabetic woman, presented with one month -rapidly –extensive, 1 to 10 cm skin necroses of the trunk, limbs and eyelids. Few days after her admission, she developed dyspnoea. Chest X-ray showed an interstitial and alveolar syndrome with multiple excavated anfractuous-edged-opacities. Facial CT scan showed a right orbital cellulitis with Pansinusitis. The methamine-silver stains on a cutaneous biopsy showed filamentous septate fungal hyphae with branches at right angles. The immunofluorescence with an anti-aspergillus serum was positive. The diagnosis of secondary disseminated aspergillosis to a primary pulmonary focus with cutaneous, sinusal, and upper airway's dissemination was made. The patient died despite an intravenous amphotericin B therapy.
Conclusion : This report emphasizes the importance of evoking and seeking for a mycosis in every skin necrotic and ulcerative lesions occurring in an immunocompromised patient. The prognosis depends on the diagnosis and treatment institution delay.

Mots-clés
Aspergillose cutanée - diabéte

Key-words
Cutaneous aspergillosis – diabetes

داء الرشاشيات الجلدي ، الرئوي و الجيبي عند مريضة مصابة بداء السكري

الباحثون : ع .خالد ، ب .فازع ، د .عمار ، ع .بوزقرو ، س .بوبكر ، م .ر .كمون

تستعرض دراستنا حالة مريضة عمرها 60 سنة مصابة بداء السكري و أصيبت بداء الرشاشيات في الجلد و الرئتين و الجيوب تطور بسرعة نحو الوفاة بالرغم من علاج بالأنفوتريسين B .

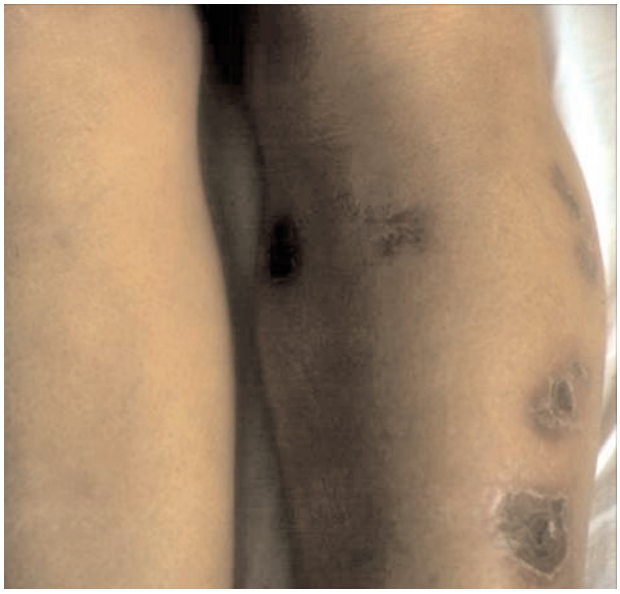
الكلمات الأساسية : داء الرشاشيات الجلدي - داء السكري

Cutaneous aspergillosis is a rare cause of skin necroses that generally occurs in immunocompromised hosts. Diabetes mellitus has been rarely implicated in the occurrence of aspergillosis.
We report here a case of multiple skin necroses due to disseminated lethal aspergillosis with pulmonary and sinusal involvement in a diabetic woman.

CASE REPORT

A 60-year-old woman, having in her past medical history diabetes mellitus, was referred to our department for cutaneous necroses that have appeared one month before her admission. Clinical examination revealed infiltrated papulo-nodular lesions that have rapidly evolved into 1 to 10 cm-necroses with round or polycyclic ulcerations (Fig 1).

Figure 1 : Skin necroses of the legs



These lesions were localized on the trunk, limbs and eyelids. On the arms, ligaments were visible because of the deepness of the ulcerations (Fig 2). Velar ulcerations with false membranes were also seen. The remaining physical examination was initially normal. On biology, blood cell count was normal. Sedimentation rate was of 32 mm (H1) with an elevated C-reactive protein (CRP=101 mg/l). There were hyper·2 globulinemia with normal gammaglobulinemia. Renal and hepatic functions were normal. There was an elevated serum glucose value requiring an insulin-therapy. Immunological study was negative (Antinuclear antibodies, ANCA, Antiphospholipid antibodies, cryoglobulins). HIV, Hepatitis B and C serologies were negative. Initially chest X-ray showed interstitial opacities of the bases. Few days after her admission, the patient had developed dyspnoea. On chest X-ray she had an interstitial and alveolar syndrome with multiple excavated anfractuous-edged-opacities. Facial CT-scan showed a right orbital cellulitis and a Pansinusitis without venous thrombosis or encephalitis. Arterial Doppler of the lower and upper limbs was normal. Histological examination of a skin biopsy showed under an ulcerated epidermal hyperplasia, a dermal necrotic material (Fig.3A) with neutrophilic abscesses, inflammatory granulomatous lympho-histiocytic infiltrate and vascular thrombosis (Fig.3B, 3C). The Gomori-Grocott stain showed filamentous septate fungal hyphae with branches at right angles. The immunofluorescence with an anti-aspergillus serum (Antibody DAKO) was positive (Fig 4). There was no fluorescence with anti-mucor serum. The diagnosis of secondary disseminated aspergillosis with primary pulmonary focus and cutaneous, sinusal, and upper airways dissemination was made. The patient died few days despite the onset of an intravenous amphotericin B treatment at a dose of 1 mg/kg/day.

Figure 2 : Deep ulcerations of the arm with visible ligaments

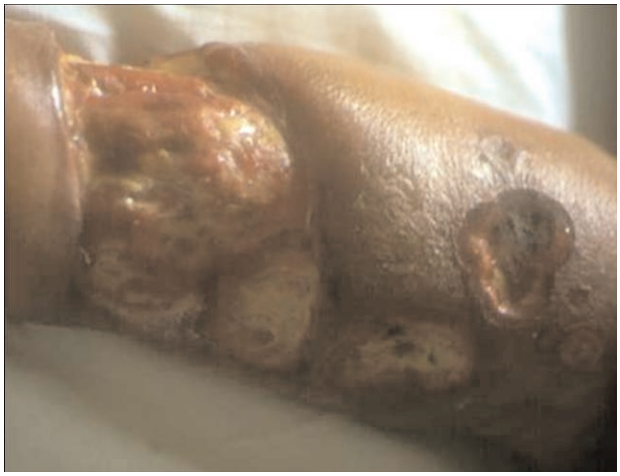


Figure 3 : 3A: Ulcerative and hyperplasic epidermis with necrotic material of the dermis

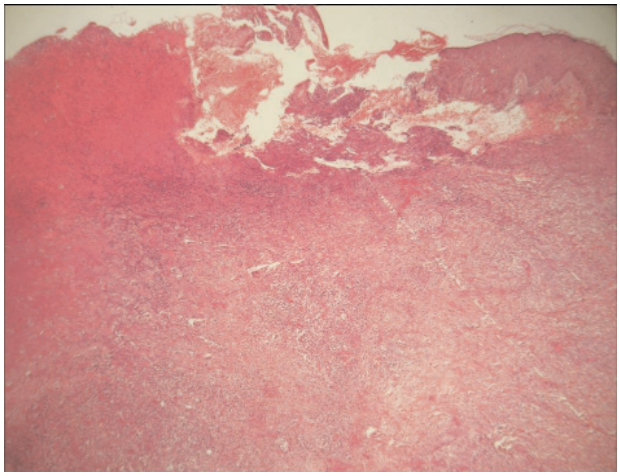


Figure 3 : 3B, 3C: Neutrophilic abscesses and inflammatory granulomatous and lympho-histiocytic infiltrate with vascular thrombosis

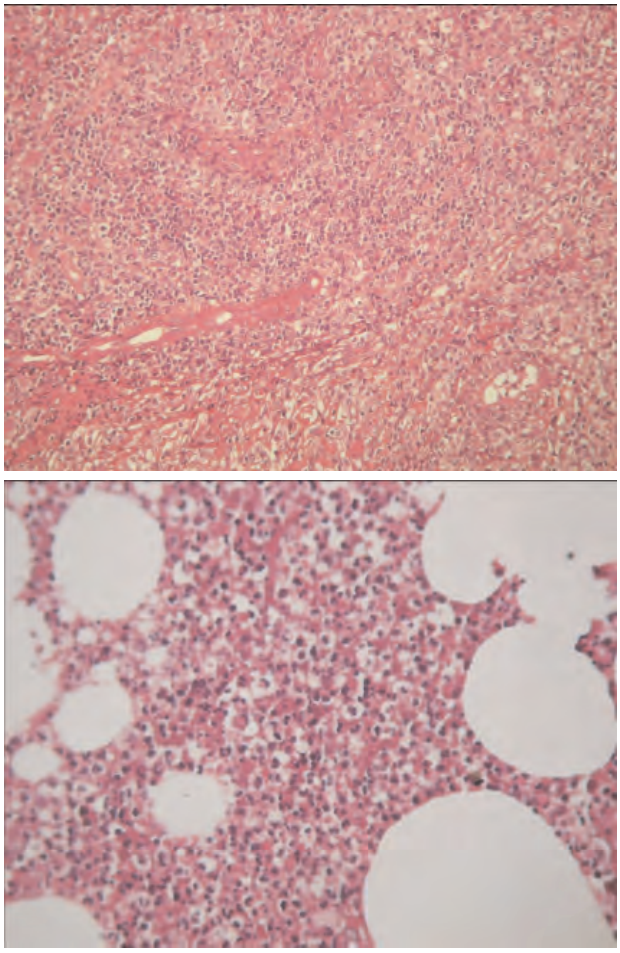
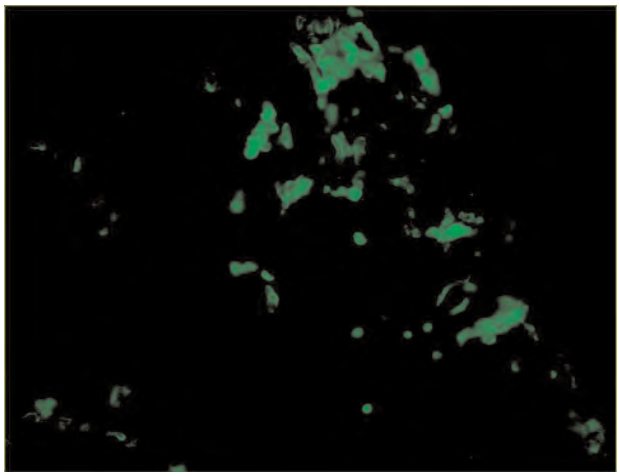


Figure 4 : Positive immunofluorescence with anti-aspergillus serum (Antibody DAKO)



DISCUSSION

This report emphasizes the importance of evoking and seeking for a mycosis in every skin necrotic and ulcerative lesion occurring in an immunocompromised patient.

Aspergillus spp (A) is a saprophytic fungus, common in soil, water, decaying vegetation, and any substrate that contains organic debris. The spores entered organism by inhalation (1, 2). Only five species have been reported to cause human infection: A. fumigatus, A. flavus, A. Niger, A. terrus, and A. nidulans.

A. fumigatus is the most common cause of disseminated aspergillosis and A. flavus is more often associated with primary cutaneous involvement (2). In immunocompromised patients, they constitute frequent opportunistic pathogens after candida. Various conditions may predispose to aspergillosis, especially granulocytopenia, haematological disorders, neonatal period, cutaneous injury or burns, systemic corticosteroids, chemotherapy, and immunosuppression (1, 2). Diabetes is rarely reported as a causative factor of invasive aspergillosis with cutaneous localization (3, 4).

More rarely, Aspergillosis has been reported in immunocompetent patients (5, 6). Aspergillosis may be located in lungs, central nervous system or nasal-orbital area or may be disseminated. Cutaneous aspergillosis is a rare condition. It can be primary, occurring by inoculation from an intravenous catheter, a macerative skin after the use of adhesive tape or surgical scar or burns. It can also be secondary to haematogenous dissemination. As illustrated by the case observed, primary infection site is generally the lung. Finally, cutaneous aspergillosis may arise from direct invasion of the skin from an infected adjacent structure, such as the nose or sinuses (6, 7). Physiopathologically, Aspergillus is responsible of angiitis of small and large vessels and a subsequent haemorrhagic infarction and necroses facilitating the extension and the formation of abscess. This mechanism explains the preferential distribution of the lesions in areas of terminal circulation like limbs and head and the absence of lesions in the trunk.

The diagnosis of invasive aspergillosis constitutes a diagnostic challenge leading as in our case to multiple biological explorations to rule out the other aetiological factors of skin necroses especially immunological origins. In fact, cutaneous lesions represent an important site for biopsy and culture, allowing a rapid diagnosis and limiting the need for more invasive procedures.

Rapid and routine mathamine-silver (Gomori-Grocott) stains lead to diagnosis by showing the septate fungal hyphae with the typical dichotomous branching of Aspergillus spp. As for the case observed, the immunofluorescence using monoclonal or polyclonal antibodies specific of species can also contribute preciously to the diagnosis. The treatment of choice of aspergillosis is early institution intravenous amphotericin B (2). Itraconazole seems to be as effective as amphotericin B with fewer side effects. Other treatments have been successfully

used like, voriconazole, potassium iodide, 5-fluorocytosine, fluconazole, terbinafine, and granulocyte colony stimulating factor (G-CSF) (8). Surgical removal can be used in sinusal aspergillosis (2). Invasive aspergillosis constitutes a therapeutic emergency. Its prognosis depends on the diagnostic delay and thus on the delay of antifungal institution (9).

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